

Answer to Ophthalmproblem *continued from page 1023*

2. Basal cell carcinoma

Basal cell carcinoma (BCC) accounts for 80% to 90% of skin cancers and is the most common periocular malignancy.^{1,2} It is slow growing, locally invasive, and arises from the basal cells of the epidermis. Because BCC rarely metastasizes, any associated morbidity is usually caused by local invasion, tissue destruction,^{2,3} and cosmetic disfigurement. Early diagnosis and treatment are vital and result in better outcomes. Neglected or incompletely resected tumours can invade the orbit and cause loss of vision or even loss of the eye. Extension into the paranasal sinuses or cavernous sinus can be life threatening.

In the periocular region, BCC mostly occurs at the lower eyelids, followed by the medial angle of the eyes, the upper eyelids, and the lateral angle of the eyes.⁴ Demographic features that increase the risk of developing BCC include increasing age, fair skin (types 1 and 2), light hair, and blue eyes.¹⁻³ Basal cell carcinomas that occur in younger patients tend to be more aggressive and have shorter latency periods.² Other risk factors include history of sunburn during childhood, sun exposure and skin damage, immune dysfunction, exposure to inorganic arsenic, previous BCC, and family history of skin cancer.^{3,5,6} Interestingly, a study has suggested that dietary fats might also play a role in the development of BCC.⁷

Clinical presentation

Clinically, BCC can present as asymptomatic or minimally symptomatic lumps on the skin or as lesions that bleed and scab over repeatedly.² Distortion of the eyelids, loss of eyelashes (milphosis), whitening of eyelashes (poliosis), and abnormal texture or colour might also be observed. Diagnostic suspicion is usually clinical, aided by good lighting and magnification³; however, diagnosis must be confirmed by histopathology. Biopsy is commonly employed for lesions that are accompanied by loss of eyelashes, ulceration, invasion or destruction of normal anatomy, irregular borders, distortion of eyelid margins, and bleeding. In cases in which deeper spread is suspected, imaging techniques such as magnetic resonance imaging or computed tomography are employed.³ Differential diagnoses include benign eyelid masses (eg, seborrheic keratosis, cysts, nevi, hordeolum, chalazia, mulluscum contagiosum, actinic keratosis, and squamous papilloma)⁸ and other malignant lesions (eg, squamous cell carcinoma and sebaceous cell carcinoma).

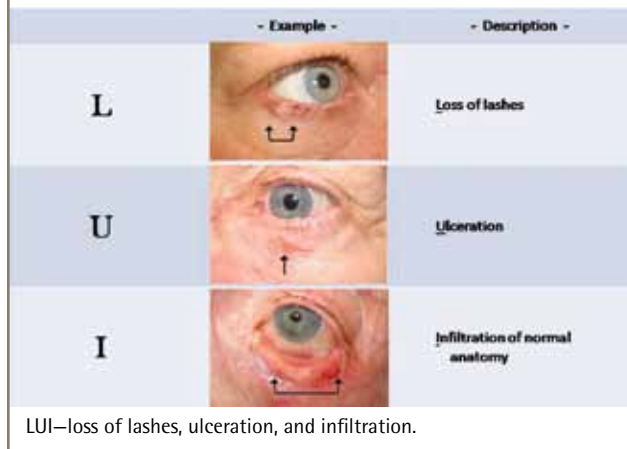
Because of the variability in presentation, up to 40% of eyelid lesions might be clinically misdiagnosed. This can lead to delay in treatment and increased morbidity in the long run. Studies have shown that such false-negative results of clinical judgment occur at all levels of training and specialization, from family medicine to ophthalmic

plastic surgery.⁹⁻¹¹ In order to decrease the rate of potential clinical misdiagnosis of a malignant lesion as benign, Dr Kratky from the Department of Ophthalmology at Queen's University in Kingston, Ont, developed a screening tool to aid in the decision-making process at the primary care level.^{12,13} Three clinical features are most consistently predictive of a malignant process upon clinical evaluation: "loss of lashes," "ulceration," and "infiltration" of normal anatomy.¹⁴ Together they comprise the "LUI key" for triaging eyelid lesions (**Figure 1**). (The term *infiltration* also encompasses destruction or replacement of normal tissue.) If any of these 3 features is present, the lesion is suspicious; either a biopsy should be performed or the patient should be referred to another specialist.

There are several forms of BCC; however, the localized nodular form comprises approximately 75% of all cases (C. Leung, H. Hollands, and V. Kratky, unpublished data, 2010). It is typically a firm and indurated mass, with telangiectatic vessels in the periphery. As the tumour grows, the blood supply to the centre might be compromised, leading to necrosis and a central ulcer with pearly, rolled margins.^{1,2} If the lesion is hyperpigmented, it might be incorrectly diagnosed as a malignant melanoma¹⁴; nodular BCC lesions have a predictable and less aggressive clinical course.¹

Morpheaform BCC is the next most common subtype, comprising 15% of all cases. It is usually a whitish-pink or yellow plaque with indistinct borders.^{2,8} It can also present with vague symptoms, such as blepharitis or ocular discomfort, without a clinically apparent mass.¹ It rarely ulcerates but can invade deep into the dermis and even into the orbit or paranasal sinuses.² Owing to the indistinct borders, incomplete excision of the tumour and subsequent recurrence can occur.

Figure 1. The LUI key for triaging eyelid lesions: *The presence of any of these features (ie, loss of lashes, ulceration, or infiltration) indicates that the lesion is suspicious for basal cell carcinoma.*



Other subtypes include cystic BCC and superficial multifocal BCC. The former can be misdiagnosed as a simple epithelial cyst,¹ whereas the latter presents as a diffuse area of involvement, with several lobules of tumour.^{1,2} Several syndromes have been associated with BCC. For example, basal cell nevus syndrome and paraneoplastic acrokeratosis syndrome should be suspected in young patients with BCC. They are both autosomal dominant conditions characterized by multiple tumour nodules that might present as early as childhood.^{1,2} Xeroderma pigmentosum is an autosomal recessive condition in which the skin is unable to repair DNA damage caused by ultraviolet light. As a result, patients are extremely sensitive to light and might develop BCC or other skin cancers at an early age.¹

Management


Early diagnosis and treatment of eyelid BCC generally result in better overall outcomes. Therefore, the first important point of management is to perform a biopsy on suspicious lesions. The aim of treatment is to eradicate the tumour, with histologic confirmation of clear margins, while optimizing the cosmetic outcome. Surgical excision with intraoperative or postoperative histologic examination of margins is the most widely used treatment measure.^{2,3} The tumour is excised along with peripheral and deep margins of normal tissue. The size of the margins varies depending on the size and histologic subtype of the BCC. Smaller, well-defined tumours excised with a 2-mm peripheral margin completely clear the BCC in 98% of cases. In contrast, morpheic lesions are excised with a 5-mm peripheral margin to ensure a 95% clearance rate.^{15,16}

Short-term postexcision follow-up is necessary to ensure proper wound healing; at this time, patients should be counseled on basic sun protection practices.⁸ In the long term, the frequency of follow-up is highly variable across health care centres and practitioners.³ However, because previous BCC is a risk factor for developing subsequent BCC, and because recurrences caused by incomplete excision are possible (especially with morpheiform BCC), most experts agree that long-term follow-up is necessary.^{3,8}

Non-surgical treatment for BCC can be used as adjunct treatment in high-risk cases or as first-line therapy in non-surgical candidates. These treatment measures include radiotherapy, photodynamic therapy, cryotherapy, chemotherapy, and immune modulation. Although these procedures might save more tissue compared with surgery, their potential disadvantages include inability to assess margins histologically and the increased risk of complications such as scarring, contracture, eyelid malposition, and hyperpigmentation or hypopigmentation.⁶ Additionally, because the skin overlying the lower eyelid lies on an embryonic fusion plane, the risk of BCC recurrence is higher.⁶ This necessitates the employment of surgical excision with histologic control.

Imiquimod is a toll-like receptor agonist that stimulates monocytes, macrophages, and dendriform cells to promote interferon- α and other cytokines important in cell-mediated immunity. Topical immunotherapy with imiquimod 5% cream is already approved for the treatment of BCC on the trunk, neck, and extremities. There is currently insufficient data to confidently recommend its use in the treatment of periocular BCC³; however, a small study that used imiquimod to treat nodular BCC of the eyelid in 5 patients reported positive cosmetic outcomes.¹⁷ Therefore, it is possible that with further research in oculoplastics, imiquimod might be a viable option in low-risk eyelid BCC for which good follow-up care can be established.

Conclusion

Basal cell carcinoma of the periocular skin is a common cutaneous malignancy that rarely metastasizes. If left untreated, it can invade extensively into local structures resulting in substantial morbidity, including loss of the eye. If the condition spreads into the sinuses or the orbit (and the brain), it can be fatal. Basal cell carcinoma is diagnosed by biopsy and is most often treated with surgical excision and histologic confirmation of clear margins. Patients should be monitored for recurrence and counseled about sun safety. Physicians must always have a high index of suspicion when assessing eyelid lesions. Application of the LUI key (**Figure 1**) when assessing any eyelid lesion can aid in earlier diagnosis and management. 

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Competing interests

None declared

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